THE REJECTIONS UNDER 35 U.S.C. § 102/§103

The Office Action rejects claims 28-31, 37, 38, 40, 56 and 57 under 35 U.S.C. § 102, or in the alternative under 35 U.S.C. § 103, as being unpatentable over Shepard et al. (J. Clin. Immunol., 11(3):117-127 (1991)).

The Office Action rejects claims 28-31, 37, 38 and 40 under 35 U.S.C. § 102, or in the alternative under 35 U.S.C. § 103, as being unpatentable over Lewis et al. (Cancer Immunol. Immunother., 37:255-263 (1993)).

The Office Action rejects claims 32-36, 39 and 58 under 35 U.S.C. § 103 as being unpatentable over Shepard et al. in view of Fendly et al. (Cancer Res., 50:1550-1558 (1990)), Deshane et al. (J. Invest. Med., 43 Suppl. 2:328A (1995)), and further in view of Senter et al. (U.S. Patent No. 4,975,278).

The Office Action rejects claims 42-55 under 35 U.S.C. § 103 as being unpatentable over Shepard et al. in view of Lewis et al. and Fendly et al., and further in view of Deshane et al. and Senter et al.

As a basis for all of the above rejections, the Office Action asserts:

> The instant claims utilize the open language "comprising" in delineating the method steps. Such language encompasses induction of apoptosis which is taught in the instant specification as one of the mechanisms by which the claimed antibodies induce cell death, but the scope of the claim is not restricted only to apoptosis, nor is the language restricted as to the use of other reagents, such as complement, phagocytic cells, cytotoxic drugs, or growth inhibitory agents, in addition to the antibodies. The specification teaches that antibodies 7C2 and 7F3 bind to Domain 1 of ErbB2 and that antibody 4D5 binds to ErbB2 but not to Domain 1.

Applicants submit that the claims are patentable over the cited references. A claim is anticipated under 35 U.S.C. § 102 only if each and every element as set forth in the claim is found in a single prior art reference. Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as

complete detail as is contained in the...claim." Richardson v. Suzuki Motor Corp., 9 USPQ2d 1913 (Fed. Cir. 1989). Furthermore, the prior art must be enabling and must describe the claimed invention sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention. In re Paulsen, 31 USPQ2d 1671,1673, (Fed. Cir. 1994).

A claimed invention is unpatentable under 35 U.S.C. § 103 if the differences between it and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. § 103(a) (Supp. 1988); see Graham v. John Deere Co., 148 USPQ 459, 465 (1966). The ultimate determination of whether an invention is or is not obvious is a legal conclusion based on underlying factual inquiries including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the prior art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence of non-obviousness. 148 USPQ at 467; Miles Labs, Inc. v. Shandon Inc., 27 USPQ2d 1123, 1128 (Fed. Cir. 1993).

"To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references (or references when combined) must teach or suggest all of the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure." MPEP § 2141, citing In re Vaeck, 20 USPQ2d 1438 (Fed. Cir. 1991).

Shepard et al. does not anticipate or render obvious the claimed invention. The claimed invention is directed to a method for inducing cell death comprising exposing a cell

which overexpresses ErbB2 to an effective amount of an isolated antibody that cross-blocks binding of antibody 7C2 or antibody 7F3 to ErbB2 (Claims 28-39 and 42-58); and a method of inducing cell death comprising exposing a cell which overexpresses ErbB2 to an effective amount of an isolated antibody which binds to ErbB2 and results in about 5-50 fold induction of annexin binding relative to untreated cells in an annexin binding assay (Claim 40).

Shepard et al. discloses that the anti-p185^{HER2} murine monoclonal antibody (muMAb) 4D5 is directed at the extracellular domain of the HER2 receptor and that the antibody has an effect as a result of modulating receptor function. (See page 117, left column, page 119, left column, and page 125, right column). Although antibodies 7F3 and 7C2 are mentioned in Shepard et al. (Table I and Table II at page 122), the reference does not enable these particular antibodies.[1] In particular, antibodies 7F3 and 7C2 were not deposited with respect

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[1] See, e.g., Reading & Bates Construction Company v. Baker Energy Resources Corporation et al., 223 USPQ 1168 (Fed. Cir. 1984) ("For the *invention* of the '903 patent to be *described* in the Smith brochure, pursuant to § 102(b), the Smith brochure itself must enable someone to practice the invention of the '903 patent. Preemption Devices Inc. v. Minnesota Mining & Mfg. Co., 732 F.2d 903, 903, 221 USPQ 841, 843 (Fed. Cir. 1984). It does not do that. The mere fact that the Smith brochure, a one-page promotional brochure, boasts the ability and results of the process of the '903 patent is insufficient, as a matter of law, to constitute an enabling disclosure of the process of the '903 patent.") See also Helifix Ltd. v. Blok-Lok Ltd., 54 USPQ 1299 (Fed. Cir. 2000), which states:

> It is well settled that prior art under 35 U.S.C. §§ 102(b) must sufficiently describe the claimed invention to have placed the public in possession of it. In re Sasse, 629 F.2d 675, 681, 207 USPQ 107, 111 (CCPA 1980); In re Samour, 571 F.2d at 562, 197 USPQ at 4; see also Reading & Bates Construction Co. v. Baker Energy Resources Corp., 748 F.2d 64, 651-52, 223 USPQ 1168, 1173 (Fed. Cir. 1984). Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his own knowledge to make the claimed invention. See In re LeGrice, 301 F.2d at 939, 133 USPQ at 373-74. Accordingly, even if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling. In re Borst, 345 F.2d 851, 855, 45 USPQ 554, 557 (CCPA 1965),cert. denied, 382 U.S. 973, 148 USPQ 771 (1966.)

to the reference and their sequences were not disclosed in the reference in such a way that a skilled person could have reproduced those particular antibodies based on the reference.

Furthermore, the present inventors have surprisingly discovered that certain anti-ErbB2 antibodies that cross-block binding of 7C2 and/or 7F3 antibodies to ErbB2 can induce cell death of an ErbB2 overexpressing cell. (See specification at page 6, lines 2-8).

Furthermore, the claims of the present invention require that the antibody be "isolated". As disclosed on page 19, lines 5-16, of the specification, an "isolated antibody" refers to an antibody that has been identified and separated and/or recovered from a component of its natural environment. Therefore, contaminant components of its natural environment that would otherwise interfere with its diagnostic or therapeutic uses are removed. Id. Shepard et al. neither teaches nor suggests that the disclosed antibody is "isolated" as in the claimed invention.

In view of the above, Shepard et al. does not teach or suggest an isolated antibody that cross-blocks binding of antibody 7C2 or antibody 7F3 o ErbB2 as is presently claimed.

Applicants further submit that Shepard et al combined with Fendly et al., Deshane et al., Senter et al., and/or Lewis et al. does not disclose or suggest the claimed invention.

Although antibodies 7F3 and 7C2 are mentioned in Fendly et al., Lewis et al. and Hudziak et al., like Sheperd et al., the references do not enable these particular antibodies. In particular, antibodies 7F3 and 7C2 were not deposited with respect to the references or their sequences were not disclosed in the references in such a way that a skilled person could have reproduced those particular antibodies based on the references. Applicants have shown that the particular 7F3 and 7C2 antibodies were not prior art as determined under 35 U.S.C. § 102. Moreover, the cited references would not render the claimed invention obvious under 35 U.S.C. §103.

Furthermore, Deshane et al. and Senter et al. add nothing to the references cited.

Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102 or under 35 U.S.C. § 103 over, Fendly et al., Lewis et al., or Hudziak et al. are respectfully requested.

CONCLUSION

In light of the above, Applicants believe that this application is in condition for allowance. Favorable consideration is respectfully requested.

If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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January 19, 2001
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DOCKET NO.: 9491-033-27

RELATED CASE STATEMENT

Serial or Patent Number	Filing or Issue Date	Status
09/266,706	March 11, 1999, claims priority to 07/705,256, May 24, 1991	Pending